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HOWSON AND HOWSON/WYETH
CATHY A. KODROFF
SUITE 210
501 OFFICE CENTER DRIVE
FT WASHINGTON, PA 19034

EXAMINER	
CARTER, KENDRA D	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/663,506
Filing Date: September 15, 2003
Appellant(s): ASHRAF ET AL.

Cathy A. Kodroff
Reg. No. 33,980
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 26, 2008 appealing from the Office action mailed December 27, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US 2002/0013335 A1	Azrolan et al.	01-2002
GB 2327611 A	Haeberlin et al.	02-1999

Madhavi et al. "Hindered Phenols", Food Antioxidants: Technological, Toxicological, and Health Perspectives, Dekker, 1996, pp. 277-293.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 U.S.C. 103(a) rejection

Claims 1-6 and 10-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azrolan et al. (US 2002/0013335 A1) in view of Haeberlin, et al. (GB 2327611 A) and in further view of Madhavi et al. (Food Antioxidants: Technological, Toxicological, and Health Perspectives, Decker, 1996).

Azrolan et al. teaches oral formulations of 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2) comprising for useful tablet formulations sodium lauryl sulfate,

polyvinylpyrrolidone, poloxamer 188, sodium dodecyl sulfate, sodium citrate, and a dry granulation (see page 4, column 1, paragraph 26, lines 10-12, 16-18, 25, column 2, line 1). For suspensions as a free base or pharmacologically acceptable salt hydroxyl-propyl-cellulose is used (see page 4, column 2, paragraph 28, lines 2-6). For sterile powders, polyethylene glycol, water, ethanol, and vegetable oils are used (see page 4, column 2, paragraph 29, lines 2-4 and 10-12). Under ordinary conditions of storage and use, the preparation contains a preservative to prevent the growth of microorganisms (see page 4, paragraph 28, lines 8-10).

In regards to claims 10-12 and 15-17, "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985), see also MPEP § 2113.

Azrolan et al. does not teach the specific wordage “water soluble polymer” or “pH modifying agent”. Additionally, the ranges of the water soluble polymer, surfactant and antioxidant are not disclosed (claims 1, 10, 15, and 20). Azrolan et al. also does not teach the specific antioxidant butylated hydroxyanisole or butylated hydroxytoluene (claims 13 and 18), nor citric acid (claim 20).

Haeberlin, et al. teaches the use of various carboxylic acids to stabilize (i.e. preserve) oral and parenteral formulations of macrolides, preferably a rapamycin (see abstract). The preferred acids include malonic acid, oxalic acid, citric acid, and lactic acid, and a 0.05% to 5% acid concentration range (which encompasses the instant invention citric acid concentration specification) with further disclosure that the preferred amount of acid may be determined by routine experimentation (see page 4, lines 15-26) is taught.

Madhavi et al. teaches that BHA is perhaps the most extensively used antioxidant in food industry (see page 277, section 5.2.2, first paragraph, lines 1-2, for example). The absorption and metabolism of BHA has been studied in rats, rabbits, dogs, monkeys, and humans. BHA was rapidly absorbed from the gastrointestinal tract in rats, rabbits, dogs, and humans, rapidly metabolized and completely excreted (see page 278, toxicological studies, lines 1-4, for example). BHT is another antioxidant used extensively in the food industry and is widely used in combination with other antioxidants such as BHA, propyl galate and citric acid (antioxidants disclosed on page 4 of the applicant's specification as acceptable antioxidants), see page 283, paragraph three, butylated hydroxytoluene, lines 1-4.

Although sodium citrate, sodium lauryl sulfate, sodium dodecyl sulfate, poloxamer, polyvinylpyrrolidone (PVP), polyethylene glycols, and hydroxyl-propyl-

cellulose are not disclosed as water soluble polymers, surfactants, or pH modifying agents, a chemical composition and its properties are inseparable. "Products of identical chemical composition can not have mutually exclusive properties." Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F. 2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In regards to the range of the antioxidant, water soluble polymer and surfactant in the composition, it is within the skill of the art to adjust concentrations to obtain desired characteristics. Since there are no reasons disclosed why the particular range of 0.001% to 3%, about 1% to about 40%, and about 1% to about 8% gives results that produce unexpected results, then the ranges of the antioxidant, water soluble polymer and surfactant are obvious to one skilled in the art to obtain. It is the normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages. See In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980) ("[D]iscovery of an optimum value of the result effective variable in a known process is ordinarily within the skill of the art." See, e.g., In re Baird, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). *In re Paterson* Appeal No. 02-1189 (Fed. Cir. January 8, 2003).

One having ordinary skill in the art at the time the invention was made would have found it obvious and motivated to formulate a composition of Azrolan et al. and the specific antioxidant butylated hydroxyanisole or butylated hydroxytoluene because Madhavi et al. teaches that BHA and BHT are extensively used antioxidants that are rapidly absorbed from the gastrointestinal tract, metabolized and completely excreted in humans (see page 277, section 5.2.2, paragraph 1, lines 1-2 and page 283, paragraph 3, butylated hydroxytoluene, lines 1-4).

One having ordinary skill in the art at the time the invention was made would have found it obvious and motivated to formulate a composition of Azrolan et al. and citric acid because Haeberlin, et al. teaches the use of various carboxylic acids to stabilize (i.e. preserve) oral and parenteral formulations of macrolides, preferably a rapamycin (see abstract). The preferred acids include malonic acid, oxalic acid, citric acid, and lactic acid in the concentration range of 0.05% to 5% (which encompasses the instant invention citric acid concentration specification) and further discloses that the preferred amount of acid may be determined by routine experimentation (see page 4, lines 15-26). Additionally, Azrolan et al. teaches that under ordinary conditions of storage and use, the preparation contains a preservative to prevent the growth of microorganisms (see page 4, paragraph 28, lines 8-10). Since, CCI-779 is a derivative of rapamycin as well as a macrolide, one of ordinary skill in the art would reasonably expect citric acid to stabilize (i.e. preserve) the composition.

The motivation for a composition comprising PVP and sodium lauryl sulfate or sodium dodecyl sulfate is because Azrolan et al. teaches that these components are useful for making tablets (see page 4, column 1, paragraph 26, line 10), suspensions (see page 4, column 2, paragraph 28, line 3), and sterile powders (see page 4, column 2, paragraph 29, lines 2-4). It would be beneficial for the applicant's composition to be made in to a tablet, suspension or sterile powder for use as a medicament. In addition, Rubino et al. states that one of skill in the art may readily select other suitable surfactants (see page 2, column 2, paragraph 21, lines 7-8). Thus, a suitable surfactant and water soluble polymer is chosen based on the type of appearance (i.e. powder, suspension, tablet) or potential use that one of ordinary skill in the art wants to make.

Double Patenting rejections

(1) Claims 1, 2-6, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 55, 58-61, 65, and 72-73 of copending Application No. 10/930,487 in view of Azrolan et al. (US 2002/0013335 A1). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The U.S. Application 10/930,487 teaches a composition comprising an amorphous form of rapamycin 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid, comprising: a metal chelator, a pH adjuster, a surfactant, at least one filler, a binder, a disintegrant, and a lubricant (see claim 55). The pH adjuster comprises citric acid, ascorbic acid, fumaric acid or malic acid (see claims 58-59). The surfactant is selected from a polysorbate, a sorbitan ester, poloxamer, or sodium lauryl sulfate (see claims 60 and 61). The binder comprises providone, hydroxypropylmethylcellulose, carboxymethylcellulose or gelatin (see claim 65). The composition is dry or wet granulated (see claims 72 and 73), and can be in the form of a tablet (see claim 74).

The U.S. Application 10/930,487 does not teach the specific wordage “water soluble polymer” or “antioxidant”, wherein the antioxidant is from 0.001% to 3% (wt/wt). Additionally, the ranges of the water soluble polymer and surfactant are not disclosed, or the use of polyvinylpyrrolidone.

Azrolan et al. teaches oral formulations of 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2) comprising for useful tablet formulations sodium lauryl sulfate,

polyvinylpyrrolidone, poloxamer 188, sodium dodecyl sulfate, and wet or dry granulation (see page 4, column 1, paragraph 26, lines 10, 11, 16-18, 25, column 2, line 1). For suspensions as a free base or pharmacologically acceptable salt hydroxyl-propyl-cellulose is used (see page 4, column 2, paragraph 28, lines 2-6). For sterile aqueous solutions or dispersions and sterile powders, polyethylene glycol, water, ethanol, and vegetable oils are used (see page 4, column 2, paragraph 29, lines 2-4 and 10-12).

One having ordinary skill in the art would find it obvious to formulate a pharmaceutical composition comprising a water soluble polymer and an antioxidant according to 10/930,487 because hydroxypropylmethylcellulose (see claim 72) is a water soluble polymer and ascorbic acid (see claim 58) is an antioxidant. "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F. 2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In regards to the range of the antioxidant, water soluble polymer and surfactant in the composition, it is within the skill of the art to adjust concentrations to obtain desired characteristics. Since there are no reasons disclosed why the particular range of 0.001% to 3%, about 1% to about 40%, and about 1% to about 8% gives results that produce unexpected results, then the ranges of the antioxidant, water soluble polymer and surfactant are obvious to one skilled in the art to obtain.

One having ordinary skill in the art would find it obvious to formulate a pharmaceutical composition comprising polyvinylpyrrolidone (PVP) because Azrolan et al. teaches a composition comprising 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2) comprising for useful tablet formulations polyvinylpyrrolidone (see page 4, column 1, paragraph 26, lines 10, 11, 16-18, 25, column 2, line 1). Thus, the specific water soluble polymer, PVP, has been taught in combination with the Applicant's compound in a solid preparation.

(2) Claims 1, 2-6, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-8 and 11 of copending Application No. 11/030,685 in view of Azrolan et al. (US 2002/0013335 A1). This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The U.S. Application 11/030,685 teaches a composition comprising micronized CCI-779, surfactant, filler/binder, disintegrant (see claims 1 and 7), one or more antioxidants, a chelating agent, and/or a pH modifier (see claim 11). The surfactant is

sodium lauryl sulfate (see claim 8). An oral CCI-779 dosing unit comprises citric acid at 0.08% w/w, BHT at 0.05% w/w, BHA at 0.022% w/w (see claim 23), and 2% w/w hydroxypropylmethylcellulose (see claim 26). The dosing unit is selected from the group consisting of a tablet and a capsule (see claim 27).

The U.S. Application 11/030,685 does not teach the specific wordage "water soluble polymer" or a composition comprising a granulation. Additionally, the specific water soluble polymer, polyvinylpyrrolidone (PVP) and its amounts are not disclosed.

One having ordinary skill in the art would find it obvious to formulate a pharmaceutical composition comprising a water soluble polymer and a composition comprising a granulation according to 11/030,685 because hydroxypropylmethylcellulose (see claim 26) is a water soluble polymer and the composition is in granular form due to formation of a tablet (see claim 27). "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F. 2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

One having ordinary skill in the art would find it obvious to formulate a pharmaceutical composition comprising polyvinylpyrrolidone (PVP) because Azrolan et

al. teaches a composition comprising 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2) comprising for useful tablet formulations polyvinylpyrrolidone (see page 4, column 1, paragraph 26, lines 10, 11, 16-18, 25, column 2, line 1). Thus, the specific water soluble polymer, PVP, has been taught in combination with the Applicant's compound in a solid preparation.

In regards to the range of the PVP, it is within the skill of the art to adjust concentrations to obtain desired characteristics. Additionally, the water soluble polymer, hydroxypropylmethylcellulose is in the composition in about 2% w/w (see claim 26). Thus, it would be obvious to comprise the composition with the same amounts of a different water soluble polymer. Since there are no reasons disclosed why the particular range of about 5% to about 20% wt/wt gives results that produce unexpected results, then the ranges of the water soluble polymer are obvious to one skilled in the art to obtain.

(3) Claims 1, 2, 4, and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-16 and 19 of copending Application No. 10/626,943. This is a <u>provisional</u> obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The U.S. Application 10/626,943 teaches a parenteral formulation (see claim 12) which comprises an antioxidant, propylene glycol (see claim 15), citric acid (see claim 14), a surfactant (see claim 12), ethoxylated vegetable oil, and polyoxyethylene-polyoxypropylene block copolymers (see claim 16). The antioxidant comprises from about 0.0005 to 0.5% w/v of the formulation.

The U.S. Application 10/626,943 discloses range of the antibiotic is w/v, whereas the applicant discloses the antibiotic range in wt/wt. The different measurements are viewed as the same to one ordinarily skilled in the art. The w/v measurements are taken in regards to the co-solvent concentrate, which is water (see claim 15). Since water has a density of 1 g/mL, and the weight of the applicant's composition is taken as a whole (i.e. 1), then the measurements are virtually the same.

The U.S. Application 11/030,685 does not teach the specific wordage "water soluble polymer" or a composition comprising a solid granulation. Additionally, the ranges of the water soluble polymer and surfactant are not disclosed.

Although citric acid is disclosed as an antibiotic and polyethylene glycol is disclosed as a dilute solvent, a chemical composition and its properties are inseparable.

"Products of identical chemical composition can not have mutually exclusive properties." Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F. 2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In regards to the range of the water soluble polymer and surfactant in the composition, it is within the skill of the art to adjust concentrations to obtain desired characteristics. Since there are no reasons disclosed why the particular range of about 1% to about 40%, and about 1% to about 8% gives results that produce unexpected results, then the ranges of the antioxidant, water soluble polymer and surfactant are obvious to one skilled in the art to obtain.

One having ordinary skill in the art would find it obvious to formulate a pharmaceutical composition comprising a solid granulation because it is a species of the genus parental formulation (see claim 12). In other words, a parental formulation can be in a solid granulation and since there are no reasons disclosed why the solid granulation form gives results that produce unexpected results, then the solid granulation form is obvious to one skilled in the art to obtain.

(10) Response to Argument

Claims 1-6 and 10-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azrolan et al. in view of Haeberlin, et al. and in further view of Madhavi et al.

> The Appellant argues that none of the cited references would lead one of skill in the art to the solid CCI-779 compositions presently claimed. None of these documents recognizes the problem to which the present invention is directed. The Examiner has not provided any motivation to combine these documents to arrive to the claims presently pending other then through hindsight. The Examiner's assertion that one would combine Azrolan with Madhavi because BHA and BHT are extensively used antioxidants fails to supply any actual reason to combine. Similarly, that Haeberlin describes the use of acids to stabilize macrolides does not itself supply any motivation to combine with Azrolan. Even if combined, the determination of what percentage of each component to include in the composition could not be derived from these documents because it is inventive selection of components and amounts of same in order to solve the problems identified by the Appellant. Further, the Examiner can identify no parallel standard variables in *In re Boesh* that would render Appellants' work a mere optimization.

The Examiner disagrees because first, the motivation to combine the elements of the composition does not have be the same as the Appellants' reasons to combine. In regards to the obviousness to combine the prior art references, such as a specific suggestion or teaching in the cited references, the KSR forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. See the recent Board decision EX parte Smith, --USPQ2d--, slip op. at 20, (Bd. Pat. App & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1396) (available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf). Nevertheless, reasons for motivation were given in the previous office action and repeated by the Examiner above.

Specifically, Azrolan et al. teaches an oral formulation of 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2) as a dry granulation in tablet form comprising surfactants such as sodium lauryl sulfate and sodium dodecyl sulfate, polyvinylpyrrolidone, poloxamer 188 (i.e. water soluble polymers), surface modifying agents such as sodium citrate (i.e. pH modifying agent; see page 4, column 1, paragraph 26, lines 10-12, 16-18, 25, column 2, line 1), and an antioxidant (see claims 7, 14 and 21). The composition must be stable under the conditions of manufacture and storage and must be preserved against contamination action of microorganisms such as bacteria and fungi (see page 4, paragraph 29, lines 6-9). Under ordinary conditions of storage and use, the preparation contains a preservative (i.e. antioxidant) to prevent the growth of microorganisms (see page 4, paragraph 28, lines 8-10). Therefore, Haeberlin et al. provides the teaching that macrolide formulations, preferably rapamycin (see abstract) are stabilized with 0.05% to 5% concentration range of citric acid (see page 4, lines 15-26), thus providing motivation for including citric acid in the formulation of Azrolan et al. In regards to the specific antioxidants BHT and BHA claimed by Appellant in claims 13 and 18, Madhavi et al. provides the teaching that these antioxidants are commonly used and combined with other antioxidants such as citric acid (see page 283, paragraph 3, butylated hydroxytoluene, lines 1-4; and page 277, section 5.2.2, first paragraph, lines 1-2). One advantage of BHA is that is rapidly absorbed from the gastrointestinal tract, metabolized, and excreted (see page 278, toxicological studies, lines 1-4). Therefore,

since the formulation of Azrolan et al. comprises a preservative and an antioxidant, Madhavi provides motivation of why one skilled in the art would use BHA or BHT as the antioxidant or preservative.

In regards to the Appellant's arguments about amounts, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.) Haeberlin teaches 0.05-5% of citric acid and Azrolan et al. incorporates by reference amounts of surface modifying agents (i.e. surfactants and water soluble polymers) such as polyoxamer 188, PVP (i.e. polyvinylpyrrolidone) and sodium dodecyl sulfate that are known in the art (see page 4, paragraph 26, column 2, lines 6-9). Thus, it is within the skill of one in the art to determine the ranges of the surfactant, water soluble polymer, and antioxidant.

In response to Appellants' argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Claims 1, 2-6, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 55, 58-61, 65, and 72-73 of copending Application No. 10/930,487(now patent number 7,271,177) in view of Azrolan et al. (US 2002/0013335 A1).

> The Appellant argues that Application 10/930,487 claims are drawn to formulations containing amorphous CCI-779 and Azrolan describes methods of treating cardiovascular disease with rapamycin which may include CCI-779, and includes general information regarding excipients useful in the formulation is provided. There is no motivation to combine Azrolan with copending Application 10/930,487. In contrast, the present application contains claims to CCI-779 with the specified excipents. One skilled in the art would not modify the specific formulation claimed in patent '177 by removing a number of required components in view of Azrolan. Also, one skilled in the art would not modify the formulations of patent '177 using a teaching of the earlier-published Azrolan application in order to arrive at the pending claims.

The Examiner disagrees because Azrolan et al. teaches oral formulations of 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2), which reads on all forms of CCI-779. Additionally, the presently rejected claims do not limit the form of CCI-779, thus the claims read on all forms of the compound. Azrolan et al. is used provide teaching of PVP, which is not taught in the patent '117 claims. Since both compositions of the current application and patent '117 "comprise" several components, either composition can further comprise components that are not claimed. Thus, the required components of patent '177 need not be removed to arrive to the current applications composition. In regards to the use

of Azrolan et al. to modify the formulations of patent '177, Azrolan et al. is considered to be prior art for the very reason that it was published before patent '177 and is relevant to the subject matter of the patent. Thus, one skilled in the art would use the Azrolan et al. reference to modify the formulations of patent '177.

Claims 1, 2-6, and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-8 and 11 of copending Application No. 11/030,685 in view of Azrolan et al. (US 2002/0013335 A1).

> The Appellant argues that Application 10/930,487 claims are drawn to formulations containing micronized CCI-779 and Azrolan describes methods of treating cardiovascular disease with rapamycin which may include CCI-779, and includes general information regarding excipients useful in the formulation is provided. There is no motivation to combine Azrolan with copending Application 10/930,487. In contrast, the present application contains claims to non-miconized CCI-779 with the specified excipients. There is no further explanation other than a conclusory statement in regards to the ranges of the components claimed by the Appellants'. Additionally, having read the specification of the '685 application, one of skill in the art would be lead away from the claimed compositions comprising a granulation. Further, the use of hydroxypropylmethylcellose in application '685 is actually within a seal coating and the reference to the composition being in a tablet form does not imply that the composition is in a granular form.

The Examiner disagrees because Azrolan et al. teaches oral formulations of 42-ester with 3-hydroxy-2-(hydroxymethyl)-2-methylpropionic acid (see claim 5 and page 4, column 1, paragraph 26, lines 1-2), which reads on all forms of CCI-779. Additionally, the presently rejected claims do not limit the form of CCI-779, thus the claims read on all forms of the compound.

In regards to the Appellant's arguments about amounts, it is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955.) Azrolan et al. incorporates by reference amounts of surface modifying agents (i.e. surfactants and water soluble polymers) such as polyoxamer 188, PVP (i.e. polyvinylpyrrolidone) and sodium dodecyl sulfate that are known in the art (see page 4, paragraph 26, column 2, lines 6-9). Thus, it is within the skill of one in the art to determine the ranges of the surfactant and water soluble polymer.

In regards to the application '685 teaching away from a granulation in the specification, the Examiner did not consider the specification but the claims in the double patenting rejection. Thus, the claims do not teach away from the formulation being in a dry granulation. In regards to the application '685 not implying that a tablet is in granular form, the Examiner reads the claims on its broadest interpretations and thus one skilled in the art can formulate a granular form of a composition into a tablet. This is in comparison to if the application '685 only taught in the claims that the formulation was in a liquid form. Thus, the fact that application '685 can be formulated into a tablet, implies that the formulation can be in granular form.

In regards to hydroxypropylmethylcellose not being in the composition but in a seal coating, the Examiner agrees, but other water soluble polymers such as povidone

(i.e. PVP, polyvinylpyrrolidone) and poloxamer 188 are also disclosed in the composition of '685 (see claims 21, 23 and 24). Thus, water soluble polymers are taught in the composition of '685.

Claims 1, 2, 4, and 6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12-16 and 19 of copending Application No. 10/626,943

> The Appellant argues that the copending application no. 10/626,943 contains claims drawn to parenteral formulations comprising CCI-779. In contrast, the present application contains claims to composition of CCI-779 in a solid oral granulation. The term parenteral does not lead one of ordinary skill in the art to prepare solid pharmaceutical compositions of solid compositions for oral administration because the definition of parenteral excludes oral administration. Thus, an oral solid granulation formulation is not a species of the genus parenteral formulations.

The Examiner disagrees because one skilled in the art can formulate compositions into different forms of administration such as oral, parental, or injection based on common knowledge within the art. The main difference in the composition claims of the presently rejected claims and co-pending application 10/626,943 is the form of administration. Therefore, although parenteral formulations exclude oral formulation, it is well within the art to formulate compositions into other forms of administration.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1617

Conferees:

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616

/Kendra D Carter/

Examiner, Art Unit 1617